

Report on the Safety of *Caralluma fimbriata* and its Extract

Harry G. Preuss M.D., M.A.C.N., C.N.S.

Professor of Physiology, Medicine and Pathology

Georgetown University Medical Center

Washington, D.C. 20057

Source of Information

Much background material on *Caralluma fimbriata* was supplied by Gencor Pacific Company. This information proved useful, especially their safety reports on *Carallum fimbriata*. Additional information was obtained from PubMed and off the internet from Google.

Description

Caralluma fimbriata, also known as *Caralluma ascendens*, belongs to the family ASCLEPIADACEAE. In western India it is also called *Ranshabar*, *Makad shenguli*, *Kallimudayan*, and *Shindala makadi* (1). There are other species of *Caralluma* that grow in India. Among these are: *C. indica*, *C. attenuata*, *C. umbellata*, and *C. stalagmifera*. All these varieties of *Caralluma* are botanically and phytochemically similar to *C. fimbriata* and regularly consumed by the native population across India (1).

Background of *Caralluma* Species

Caralluma fimbriata is a tender succulent that is found in the wilds of Africa, the Canary Islands, Arabia, southern Europe, Ceylon, and Afghanistan (2,3). The *Caralluma* genus of cacti is included among those listed as edible, because the daily diets of numerous natives of India over many centuries include this edible, wild, succulent cacti (1,4,5). Daily consumption is largely due to the fact that the *Caralluma* genus grows ubiquitously in that area. *Caralluma fimbriata* is the most prevalent of the genus, as it grows wild in urban centers, is planted as a roadside shrub, and is commonly used as a boundary-marker in

gardens. This so-called vegetable is eaten daily in several different forms – cooked as a regular vegetable, placed in preserve like chutneys and pickles, and sometimes eaten raw. To give specific examples, (1) *Carulluma fimbriata* is consumed daily as a vegetable in the Kolli Hills of South India; (2) it is used in pickles and chutney in the arid regions of Andhra Pradesh; and (3) in Western India, *Caralluma fimbriata* is accepted as a famine food – suppressing appetite and quenching thirst. Legend has it that hunting tribes chewed chunks of the *Caralluma* cactus to suppress hunger and thirst when on a long hunt. Most importantly to determine safety, there are no adverse event reports on the Indian subcontinent over the centuries of use (1). *Caralluma fimbriata* is listed as a vegetable in The Wealth of India, the Indian Health Ministry's comprehensive compilation on medicinal plants (2). Key phytochemical ingredients include pregnane glycosides (6,7), flavone glycosides (8), megastigmane glycosides (8), bitter principles, saponins, various flavonoids (9), etc.

Proposed Mechanisms of Action for Weight Reduction and Safety

It is postulated that the pregnane glycosides and perhaps other constituents in *Caralluma fimbriata* prevent fat accumulation via blocking citrate lyase. This would be similar to the mechanisms proposed for another product from India, *Garcinia cambogia* (10). This is important for two reasons. The mechanism of action of *Garcinia cambogia* has proven to be safe for those desiring to lose weight (11). In addition, clues as to how *Caralluma fimbriata* works to reduce weight may emanate from our knowledge of *Garcinia cambogia*. The active component in *Garcinia cambogia* is hydroxycitrate (HCA) (10), and HCA has been reported to cause weight loss in humans without stimulating the central nervous system [12]. Because it is a competitive inhibitor of ATP-citrate lyase, an extra-mitochondrial enzyme involved in the initial steps of *de novo* lipogenesis (10). Consequently, HCA reduces the transformation of citrate into acetyl coenzyme A, a step necessary for the formation of fatty acids in the liver. In addition to its effect of citrate lyase, the postulated blocking of malonyl Coenzyme A by *Caralluma fimbriata* could further lead to a decrease in fat formation in the metabolic pathway. Again similar to *Garcinia cambogia* (10), *Caralluma fimbriata* is reported to suppress appetite

hypothesized to be secondary to effects on the appetite control center of the brain. HCA has been demonstrated to reduce food intake in animals suggesting its role in the treatment of obesity and has been demonstrated to increase the availability of serotonin in isolated rat brain cortex that could affect satiety [13-18]. More specifically, it is believed that the pregnane glycosides in *Caralluma fimbriata* inhibit the hunger sensory mechanisms of the hypothalamus.

In addition to the long history of safe ingestion of the cactus as a food, further evidence of safety of its extract is evident through an acute oral toxicity study on rats and two clinical studies. The former was carried out by the Department of Pharmacology, St John's Medical College in Bangalore, India. Doses of 2g/kg body weight and 5g/kg body weight were gavaged to rats. All animals survived until the scheduled necropsy at the end of the study period of 14 days. Histology revealed no abnormalities in the various organs. Accordingly the LD50 for the rats exceeded 5g/kg.

Clinical Studies on Weight Reduction

Clinical Trial #1

An extract prepared via an aqueous alcohol extract and containing one gram of material was developed and used in the weight loss studies. The extract dosage was based upon an attempt to duplicate the average intake of 50 grams of raw cactus a day (10-12 grams solid material). The first study performed in India consisted of 50 overweight/obese subjects (BMI >26) — 25 received active compound and 25 received a placebo. The study, under the purview of the Institutional Ethics Review Board of St John's National Academy of Health Sciences, Bangalore, India, was randomized, double-blind, and placebo-controlled. Over eight weeks, the subjects were tested for weight-loss, anthropometry, body fat composition, BMI, net weight and systemic functions. During the study, no changes were made in diet; and all subjects were advised to walk 30 minutes in the morning and evening. The adverse events were minor and limited to mild upset of the gastrointestinal tract. Importantly, they were present equally in the active and placebo groups. Constipation and flatulence subsided within a week and were attributed to the gelatin capsules more than the

ingredients from the cactus present in the capsules. Examination of fasting and post-prandial sugar, total cholesterol, LDL, HDL, triglycerides, serum creatinine, BUN, total protein, serum albumin, total bilirubin, conjugated bilirubin, AST and ALT, and alkaline phosphatase, gamma GT, and hemoglobin failed to reveal any overall toxicity from the extract (see Table 1). Blood pressure and EKG also showed no toxic reactions secondary to ingesting *Caralluma fimbriata*.

Clinical Trial #2

The second study performed in California at the Western Geriatric Research Institute consisted of 26 overweight patients, 19 on active compound and 7 on placebo. Over 60% of those taking the extract lost 6 pounds or more for the month. This study is suggestive of a positive effect of the *Caralluma fimbriata* extract on weight loss. Importantly, it reaffirmed the safety of the extract, as no serious adverse events occurred.

Other Actions of Caralluma

In folklore medicine, plants of the *Caralluma* species have been used to treat diabetes. In a study using streptozotocin diabetic mice, acute or subacute treatment with *C. arabica* caused a statistically significant lowering of circulating blood glucose levels (19). Streptozotocin-induced diabetes is a model for Type I diabetes mellitus. Accordingly, in these insulin deficient mice, the *Caralluma* species was able to lower blood glucose suggesting an “insulin-like” action, an increase in insulin release, and/or an ability to sensitize the animal to lesser amounts of insulin. However, one oddity was that in this particular study the glucose tolerance to a glucose challenge appeared better in the control animals even though baseline sugars were higher in control.¹ Similar to *C. arabica*, extracts from *C. attenuata* were found to be antihyperglycemic in alloxan-diabetic rats (20). Animal studies suggest that *C. arabica* extract is anti-nociceptive and anti-inflammatory (21,22). Using the hot plate and writhing methods in albino mice and the tail-flick method in Wistar rats, the nociceptive properties of *C. arabica* were shown. This

¹ This finding relates to therapeutic evaluation and is contrary to the other report mentioned above indicating a hypoglycemic effect predominates. Accordingly, it would not appear to influence the safety of the compound.

occurred when the extract was placed on the skin indicating transdermal absorption. The lesser accumulation of edema in the in paws injected with carageenan indicated anti-inflammatory properties as well. This property was localized to a specific pregnane glycoside from *C. umbellata* (23). *C arabica* also has been shown to possess anti-gastric ulcer and cytoprotective properties against damage produced by phenylbutazone, indomethacin, ethanol, sodium hydroxide, and/or cold restraint stress (24). The protective effect was postulated to be via multi mechanisms, including increased gastric production of prostaglandins and mucin and reduced gastric acidity.

Overall View of *Caralluma fimbriata* and Extract

I have reviewed the Gencor Pacific report on *Caralluma* and believe the information is correct and accurate. Accordingly, all current evidence points to the safety of *Caralluma fimbriata* extract at the recommended doses.

I believe that *Caralluma fimbriata* is safe to consume at recommended doses based on the following:

1. the cactus has been in the food chain of India for years and has not been associated with any significant adverse side effects.
2. *Caralluma fimbriata* is listed in the Wealth of India as a famine food and by various individuals on the internet as a safe-to-consume food
3. various testimonial by doctors and scientists confirm to its safety.
4. testimonial by individuals who regularly consume the product describe its safety
5. the daily dose of the extract contains the same concentration of ingredients as commonly eaten daily in the raw vegetable
6. a study to determine LD50 did not disclose toxicity, and it was reported that the LD50 exceeded 5g/kg
7. two clinical studies composed of 44 individuals consuming the extract failed to reveal any significant adverse events.

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